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Progress over the last year on the development of multineuronal recording systems has been significant. Since this was one of the main objectives of the consortium of three laboratories it has been a principle focus of the past years research efforts. This phase is near completion and currently being implemented in several research projects. Consequently most of the research effort in the past year has been directed toward these technological accomplishments. However in addition to the strides made in bringing the multineurone and multi-tasking computer systems to completion, several studies which were in preliminary stages at the time of submission are now near completion and are being prepared for publication. Specifically, these include the signal detection task and the DMTS task in which complex neurophysiological analyses have revealed striking new relationships to sensory processing strategies in the hippocampus and cortex. The accompanying report summarizes these and other accomplishments in the second year of the award.

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Multiple Neuron Recording in the Hippocampus of Freely Moving Animals

Progress Report for AFOSR-90-0092

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Progress Report

Summary

Progress over the last year on the development of multineuronal recording and analysis systems has been significant. This was one of the main objectives of the three laboratory consortium, and it has been a principle focus of the research efforts. The multitasking computer system has been in operation in this laboratory for the past year, and has been undergoing testing in the other two laboratories. Prototype DSP-based multineuron recording system has also been in test phase this past year pending development of the software interface for neural spike dicscrimination. Consequently most of the research effort in the past year has been directed toward these technological accomplishments. In addition, studies using the signal detection task and the DMTS task in which have revealed striking new relationships to sensory processing strategies in the hippocampus and cortex. The following report will summarize these and other accomplishments in the first year of the award.

Research Objectives: Statement of Work

The research objectives of the second year of the award were primarily: (1) to continue to develop and implement the computer system for behavioral control and multiple neuron recording in hippocampus and related structures, and (2) to utilize these techniques in sample memory tasks to determine the nature of sensory processing by the hippocampus and related structures. Each of these objectives will be dealt with in a separate section below.

Development of Multineuron Recording Technology: In the first year, this laboratory was responsible for developing a multi-tasking version of the Unitlab software (J. Chapin) for the Motorola realtime operating system (i.e. the Delta 2616 system). A version of this program (Q'Unit) providing behavioral control at 1 ms resolution was made operational by the end of the year. During the second year, electrophysiological recording concurrent with behavioral control, and variable timing were added, allowing 200 μs resolution data acquisition, and 1 ms event control. This version has been distributed to the other laboratories, and numerous tests and revisions have been performed. The software also enables the Motorola system to control and collect data from up to 8 independent stations (behavioral experimental chambers) at a time, and can handle up to 16 behavioral event controls and 64 neural spike input channels as well as 8 analog inputs and 2 analog outputs. This capability is more than double the channel numbers over the previous year, and reflects many improvements in the way the data is recorded and stored. In addition, a number of on-line graphic displays have been added to the acquisition program which allow viewing of stripcharts and perievent histograms from up to 4 experimental chambers during the actual recording session. Finally, a Motorola version of Dr. Chapin's Analyze program has been received, and interfaced to the Q'Unit acquisition program. The combination of these programs makes this an extremely powerful laboratory research package for collecting the necessary volume of physiological data from enough animals to achieve statistical significance by projected power analyses, a problem which has plagued this research field for many years.

The second major technological accomplishment in this time period has been the development of expanded the 128 channel differential input, 64 channel DSP (digital signal processing) neuron recording systems. At the end of last year, a 32 channel system was delivered, but control programming was in a very rudimentary form. Numerous testing and development iterations between the three laboratories and Spectrum Scientific, the developer, have resulted in a Microsoft Windows-based user interface which allows extensive menu and mouse-based selection of channels and spike discrimination parameters. This development has eased many technical problems with the use of this system. The DSP system is currently interfaced to the data acquisition system by a 64 bit parallel interface which allows monitoring of all DSP event outputs by any of the independent experimental stations within the Motorola system. The implementation of this device using multiwire bundle and array microprobes constitutes the final phase of technological design, fabrication, and testing which has been in process over the last 4-5 years by the three independent laboratories.

Patterned microwire arrays have been received at the end of the second project year. These arrays are designed to place recording sites at defined positions along the known anatomic projections between cell layers of the hippocampus. Recordings using these arrays will be implemneted in the third year of the project.

Personnel:

Dr. Robert Hampson, Ph.D. Research Asst. Professor BGSM.
Mr. Terrence Bunn, Advanced Systems Programmer

Signal Detection and DMTS Studies, Phase II: Progress to date on these experiments has concentrated on analyses of the behavioral correlates of hippocampal neural activity in these behavioral paradigms. In addition, work has begun on analysis and modelling o fhte hippocampal place cell firing observed during the DMTS task. These results are currently in the final stages of analysis and preparation of publication. A brief summary of the findings from each study will be presented below.

Signal Detection Task: Analyses of the hippocampal and cortical evoked potential data from the auditory signal detection and discrimination task indicate that "late" cortical potentials (i.e. 140 msec) evoked on detect vs nondetect trials (defined by behavioral criteria), do not follow the same pattern of variation as potentials recorded from the dentate gyrus as reflective of the input from the entorhinal cortex. These data indicate that the processing of sensory information and the manner in which it effects detection of tone stimuli of different intensities on subsequent trials may be a function of the prior biasing of hippocampal synaptic processes to respond to patterned inputs which have been detected by the sensory cortex. In addition, analyses of the sequential dependency of these potentials indicates a flow of information from hippocampus, to neocortex, and back to hippocampus, which may account for these differences. We have determined that the P140 cortical potential follows the hippocampal G-cell outputs, whereas one of the G-cell inputs is in turn modified on the next trial in a manner consistent with negative feedback from the neocortical P140.

Thus the completion of this phase of these studies now allows for the further modification of the signal detection paradigm to include selective information biasing of patterned sensory inputs to allow the determination of the "rules" by which such two-way interactive biases between cortex and hippocampus are produced. This will allow the implementation and adaptation of neural computational and neural network modeling to the predictive scheme for simulation of sensory information processing mechanisms.

Delayed Match to Sample Memory Task: Extensive analysis of single hippocampal neuron activity in the DMTS task has been completed in the last year. The analysis is unique in that a thorough compilation of the data from 75 different and independently verified hippocampal neurons meeting the criteria for complex spike cells have been examined in every phase of the task. Several unforseen outcomes were provided by this unique analysis strategy which gets at the heart of hippocampal cellular participation in information storage and its role in memory processes.

There are five phases to the DMTS task, sample lever presentation, sample lever response, delay interval, match lever presentation, and match lever response. We have found that identified hippocampal cells have unique response patterns in each of these phases and that different subtypes of hippocampal cells are present which selective respond to one or more of these phases of the task. This insight has allowed us to formulate a preliminary model of hippocampal cell function in the task and to simulate these processes in various neural networks portraying hippocampal circuit interactions.

A neural network model specifically designed to mimic spatial correlates of hippocampal neural activity has been completed in the past year. This model concentrates on plasticity of place fields seen on a open platform when differential rewards are given, and in the DMTS apparatus as the animal is trained in the task. The simulations provide the basis for further investigations of hippocampal involvement in memory processes by varying the nature of the DMTS task to exercise the unique properties of hippocampal neurones.

In addition, the implementation of the multineuron recording capacity and DSP cell identification procedures in conjunction with recently received microwire arrays will provide the basis for integration of the information obtained in Phases I and II, to understanding of the spatial and temporal distribution of the differential roles of particular subtypes of hippocampal cells in and their relationship to the newly described hippocampal anatomic circuitry disclosed by Amaral *et al.* (1991). Phase III of the project will be concerned with (1) extension of multineuron array recording in the DMTS task, and (2) Refinement of the models of hippocampal cellular involvement in memory and information processing.

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Ms. Jeri Meltzer, Research Technician III, BGSM
Ms. Katherine Alexander, Research Technician II, BGSM

Publications and Presentations Relevant to This Grant

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3. Hippocampal cell firing correlates of delayed match to sample performance in the rat. Hampson, R.E., Heyser, C.J., and Deadwyler, S.A. To be Submitted to Behavioral Neurobiol. 1992

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